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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/902,432	07/10/2001	Irwin Gelman	A30558-A-FWC-A	8487

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EXAMINER
PRIEBE, SCOTT DAVID

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/902,432	Gelman et al.
Examiner	**Art Unit**
Scott D. Priebe, Ph.D.	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Dec 5, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above, claim(s) *1-12 and 16-20* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *13-15* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Some references in this Office action to the instant specification are made with respect to their location in the published application, US 2002/0160002 A1

Election/Restriction

Applicant's election with traverse of group V, claims 13-15, in Paper No. 10 filed 12/5/02 is acknowledged. The traversal is on the ground(s) that groups V and VIII are directed to methods related to inhibiting cell proliferation by inhibiting cyclin D. This is not found persuasive because while the goal of the methods are similar, the products and method steps used to attain the goal are different, rendering these methods unrelated under 35 USC 121 for the reasons set forth in the restriction requirement filed 8/30/02 (para. bridging pages 3-4).

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-12 and 16-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

Priority

It is noted that this application appears to claim subject matter disclosed in prior copending Application Nos. 08/978,277, filed 11/25/97; 08/665,401, filed 6/18/96; and

08/635,121, filed 4/19/96 based upon the declaration filed 4/8/02. A reference to the prior application must be inserted as the first sentence of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). Also, the current status of all nonprovisional parent applications referenced should be included.

If the application is a utility or plant application filed on or after November 29, 2000, any claim for priority must be made during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2) and (a)(5). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) a surcharge under 37 CFR 1.17(t), and (2) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Commissioner may require additional information where there is a question whether the delay was unintentional. The petition should be directed to the Office of Petitions, Box DAC, Assistant Commissioner for Patents, Washington, DC 20231.

Applicant is reminded that in order to receive benefit of priority to an earlier filed application, the instant application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or provisional application); the disclosure of the invention in the parent application and in the second application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). Instant claims 13-15 require that the SSeCKS polypeptide bind cyclin D and prevent its nuclear translocation. As instantly disclosed, cyclin D binding is separable from other SSeCKS activities, i.e. the claims exclude SSeCKS polypeptide variants that do not bind and prevent nuclear translocation of cyclin D but retain other properties of wild typ SSeCKS. None of Application Nos. 08/978,277; 08/665,401; and 08/635,121 describe any cyclin D binding activity for SSeCKS. In the '121 application, the SSeCKS protein was implied to be a nuclear transcription factor, see col. 6, lines 32-37 of US 5,910,422, rather than a cytoplasmic and perinuclear protein associated with the cytoskeleton involved in mediating signal transduction and cytoskeletal architecture, as instantly described (e.g. see US 2002/0160002 at para. 0164). Consequently, there is no written description of the instantly claimed method in these prior applications. Should Applicant wish to obtain benefit of priority to a parent application(s), the claims should be directed to the same invention described in the parent application(s).

Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Claim 15 recites "SSeCKS polypeptide that has an increased affinity for cyclin D". The only variants of SSeCKS recited in the specification have a decreased affinity for cyclin D.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See page 90, line 10 of filed specification. The specification should be reviewed for other embedded hypertext.

The disclosure is objected to because of the following informalities:

Figure 54 (top line) discloses an amino acid sequence which is not identified by the appropriate SEQ ID NO in the "Brief Description" of the figure (see amendment of page 21, lines 8-10, filed 4/8/02. Reference to the appropriate SEQ ID NO (presumably SEQ ID NO: 4) should be made, as well as an indication of the residue numbers of the disclosed sequence(s) in the SEQ ID NO.

Page 28, line 8, refers to ATCC numbers for four strains of hybridoma. However, the ATCC numbers have not been provided. Either reference to ATCC should be deleted, or the

assigned ATCC numbers should be added. If the latter course is chosen, Applicant must provide evidence that the amended material is not new matter. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 15 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 14 is directed to a method of using a nucleic acid molecule that encodes a SSeCKS polypeptide fused to a "cytoskeletal anchoring peptide." The description of this polypeptide is limited to original claim 14, and a similar statement in the specification (see US 2002/0160002, para. 0101, 2nd to last sentence). The specification does not describe or identify any "cytoskeletal anchoring peptide." Claim 15 is directed to a method of using a nucleic acid molecule that encodes a SSeCKS polypeptide that has an increased affinity for cyclin D. However, the

description of this nucleic acid molecule is limited to original claim 15, i.e. the specification makes no mention of such a nucleic acid or polypeptide. The only variants of wild type SSeCKS described in the specification which relate to cyclin D binding have mutations in the CY motifs that greatly reduce affinity for cyclin D. See para 0293 of US 2002/0160002.

The court and the Board have repeatedly held (*Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (CA FC, 1991); *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993); *Fiddes v. Baird*, 30 USPQ2d 1481 (BPAI 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)) that an adequate written description of a nucleic acid requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it, irrespective of the complexity or simplicity of the method; what is required is a description of the nucleic acid itself. It is not sufficient to define DNA solely by its principal biological property, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any DNA with that biological property. Naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. When one is unable to envision the detailed constitution of a complex chemical compound having a particular function, such as a nucleic acid, so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the nucleic acid has been isolated. Thus, claiming all DNA's that achieve a result without defining what means will do so is not in compliance with the description requirement. Rather, it is an attempt to preempt the

future before it has arrived. The instant specification does not identify any cytoskeletal anchoring peptides, or describe such peptides in terms of their structure that would distinguish them from any other peptide. The instant specification does not disclose any SSeCKS polypeptide with higher cyclin D affinity, nor does it describe any potential method for isolating one. It provides no description of any structural characteristic which would be possessed by such polypeptides that would distinguish them from other SSeCKS polypeptides which do not have increased cyclin D affinity.

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inhibiting cell proliferation in cultured cells, does not reasonably provide enablement for inhibiting cell proliferation *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not enable one of skill in the art to practice the invention commensurate in scope with the claims. The specification suggests several utilities for the claimed invention. One utility is to inhibit cell proliferation in cell culture. The specification

does enable one of skill in the art to use the invention for that purpose. Another intended use is for gene therapy in treating cancer. The specification does not disclose any utility for practice of the method *in vivo* other than treating cancer. The specification does not enable one of skill in the art to use the invention for gene therapy or for generally inhibiting cell proliferation *in vivo*. The state of the art of gene therapy is highly unpredictable. Hence, clinical efficacy has not been demonstrated in any gene therapy protocol (see Orkin et al., page 1, ¶3), demonstrating that the state of the art of gene therapy is such that specific direction is needed. High level expression of genes transferred may not be consistently achieved (see Orkin et al., page 9, ¶2) and the frequency of gene transfer is often very low (see Orkin et al., page 2, ¶2), which demonstrates that the art of gene therapy is unpredictable. The specification does not present direction or guidance to lead one to the administration of the nucleic acid molecule, as claimed herein, to achieve expression sufficient to allow for inhibition of a transformed phenotype. In order to enable one of skill in the art to use the method as claimed specific direction is necessary with regards to the method of delivery, the dosage required for a sufficient amount of expression, and the appropriate regulatory sequences necessary to achieve such an amount of expression.

The guidance in the specification directed to gene therapy (section 5.4.2) is limited to a list of prior art delivery methods. The specification provides no new teachings on how the acknowledged inadequacies of these methods (see Orkin) can be overcome.

No working examples are presented which relate to *in vivo* administration of the nucleic acid molecule. Experiments performed with cultured cells showed that while expression of an

exogenous nucleic acid molecule encoding SSeCKS decreased proliferation of untransformed cells and *v-src* transformed cells grown in low calf serum (0.5%) media, it had no effect on proliferation of *v-src* transformed cells grown in high calf serum (10%) media (See US 2002/0160002 at para. 0202, 0208, 0211; and Lin et al., Cancer Res. 57 (11): 2304-2312, 01 June 1997). Similarly, it had no effect on proliferation of cultured MatLyLu cancer cells (see US 2002/0160002 at para. 0244; and Xia et al., Cancer Res. 61 (14): 5644-5651, 15 July 2001). These results indicate that whether expression of exogenous SSeCKS inhibits proliferation of pre-cancer or cancer cells in culture depends upon the media used, i.e. it depends upon the environment the cell is in. It is unclear from these experiments what effect expression of exogenous SSeCKS would have on tumor cells *in vivo*. MLL cells transfected *in vitro* with an SSeCKS transgene or MLL cells were implanted into nude mice. As disclosed in the instant specification, expression of the transgene had little effect on growth of the MLL/SSeCKS tumors within 8-10 days, and no effect at later time points as compared to untransfected MLL cells (see US 2002/0160002 at para. 0247). This experiment resembles an as yet unattained ideal in cancer gene therapy, delivery of a potential therapeutic gene to 100% of target cells. Yet, it had little or no effect on growth of the tumor. Thus, this result suggests that using the claimed method for inhibiting tumor growth in a cancer patient would be ineffective at best, and more probably inoperative.

With respect to claim 14, which requires a cytoskeletal anchoring peptide. As indicated in the preceding rejection, the specification does not identify any such peptides. It also provides no

guidance for making one. With respect to claim 15, the specification provides no guidance on changes that can be made to SEQ ID NO: 4 in order to increase the affinity of the SSeCKS for cyclin D, nor does it provide any working examples of such an SSeCKS polypeptide.

Therefore, given the state of the prior art, the lack of predictability in the art, the minimal amount of direction provided, the absence of applicable working examples, and the quantity of experimentation needed, the specification does not enable one of skill in the art to make and use the invention commensurate in scope of the claims without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: fusion of the SSeCKS polypeptide to the cytoskeletal anchoring peptide.

Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "increased affinity" in claim 15 is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for

ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. There is no referent by which "increased" can be determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 13 is rejected under 35 U.S.C. 102(a) and (b) as being clearly anticipated by Lin et al. (Mol. Cell. Biol. 15 (5): 2754-2762, May 1995) or Lin et al.(Cancer Res. 57(11): 2304-2312, 01 June 1997) .

Lin et al. (1995) discloses a method of inhibiting proliferation of *src*-transformed NIH 3T3 cells by transfection with a plasmid expressing the truncated SSeCKS polypeptide (SEQ ID NO: 2).

Lin et al. (1997) discloses a method of inhibiting proliferation of conditionally *src*-transformed NIH 3T3 cells by transfection with a plasmid expressing the full-length rat SSeCKS polypeptide (SEQ ID NO: 4) and growth in low calf serum media.

Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX numbers are (703) 308-4242 or (703) 305-3014 for any type of communication. In addition, FAX numbers for a computer server system using RightFAX are also available for communications before final rejection, (703) 872-9306, and for communications after final rejection, (703) 872-9307, which will generate a return receipt. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on Monday through Friday from 8 AM to 4 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

Any inquiry concerning administrative, procedural or formal matters relating to this application should be directed to Patent Analyst Patsy Zimmerman whose telephone number is (703) 308-8338. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Scott D. Priebe

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